Brain & Language 151 (2015) 35–41

Contents lists available at ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

Structural alterations of the language connectome in children with specific language impairment

Rosa Vydrova [a], Vladimir Komarek [a], Jan Sanda [b], Katalin Sterbova [a], Alena Jahodova [a], Alice Maulisova [d], Jitka Zackova [d], Jindra Reissigova [c], Pavel Krsek [a,*], Martin Kyncl [b]

[a] Department of Pediatric Neurology, Charles University, 2nd Faculty of Medicine, University Hospital Motol, Prague, Czech Republic
[b] Department of Radiology, Charles University, 2nd Faculty of Medicine, University Hospital Motol, Prague, Czech Republic
[c] Institute of Computer Science AS CR, Department of Medical Informatics and Biostatistics, Prague, Czech Republic
[d] Department of Psychology, Charles University, 2nd Faculty of Medicine, University Hospital Motol, Prague, Czech Republic

ARTICLE INFO

Article history:
Received 1 January 2015
Revised 18 September 2015
Accepted 24 October 2015

Keywords:
Specific language disorder
DTI
Arcuate fascicle
IFOF
Ventral stream

ABSTRACT

We evaluated brain white matter pathways associated with language processing in 37 children with specific language impairment aged 6–12 years and 34 controls, matched for age, sex and handedness. Arcuate fascicle (AF), inferior fronto-occipital fascicle (IFOF), inferior longitudinal fascicle (ILF) and uncinate fascicle (UF) were identified using magnetic resonance diffusion tensor imaging (DTI). Diffusivity parameters and volume of the tracts were compared between the SLI and control group. Children with SLI showed decreased fractional anisotropy in all investigated tracts, increased mean diffusivity and radial diffusivity component in arcuate fascicle bilaterally, left IFOF and left ILF. Further, bilaterally increased volume of the ILF in children with SLI was found. We confirmed previous findings indicating deficient connectivity of the arcuate fascicle and as a novel finding, demonstrate abnormal development of the ventral language stream in patients with SLI.

1. Introduction

Specific language impairment (SLI) is a developmental language disorder which hinders the mastery of language skills in children who have no obvious sensory, mental, physical or emotional deficits. It represents one of the most common childhood learning disabilities, with prevalence of approximately 7% of preschool children (Tomblin et al., 1997). SLI encompasses a heterogeneous group of speech deficits. Children with SLI have problems with receptive language (understanding), expressive language, or speech (articulation). Most individuals have deficits in structural aspects of language (lexical knowledge, syntax, phonology), others show difficulties in pragmatic aspects of language and communication (i.e. using language appropriately in social situations). Subjects with SLI have significant communication problems which may persist into adulthood. Neurobiological mechanisms underlying SLI have not been fully elucidated. Moreover, early developmental signs predicting language difficulties and enabling early diagnosis and intervention in these children have not been reliably identified.

Recent neuroimaging studies showed that language processing is supported by distinct, distributed and interacting networks connecting regions relevant for language located in the temporal and inferior frontal cortex, including Wernicke's and Broca's areas, respectively (reviewed by e.g. Dick, Bernal, and Tremblay (2013), Friederici and Gierhan (2013), Price (2012)). Increasing evidence supports the dual stream "dorsal-ventral" model (Hickok & Poeppel, 2004). Dorsal stream connects fronto-temporo-parietal cortical regions via branches of the superior longitudinal fascicle (SLF) and the arcuate fascicle (AF). Ventral stream is assumed to consist of fiber bundles including the inferior fronto-occipital fascicle (IFOF), the inferior longitudinal fascicle (ILF) and the uncinate fascicle (UF). Function of the dorsal stream has been related to mapping auditory speech sounds to articulatory (motor) representations (Saur et al., 2008) and also to processing complex syntactic structures (Friederici, 2006). Ventral stream has been proposed to subserve the semantic aspect of language, as a sound-to meaning interface by mapping sound-based representations of speech to conceptual representations (Saur et al., 2008). Processes necessary for decoding speech and extracting its meaning include perception of phonetic signals, lexical, semantic and sentence information.

* Corresponding author at: Department of Pediatric Neurology, Charles University, 2nd Medical School, Motol Hospital, V Uvalu 84, CZ 15006 Prague 5, Czech Republic.
E-mail address: pavel.krsek@post.cz (P. Krsek).

http://dx.doi.org/10.1016/j.bandl.2015.10.003
0093-934X/

Ventral stream is therefore involved in both perception and production of speech (Specht, 2013).

Few studies have investigated white matter tracts associated with language in the SLI population. Verhoeven et al. (2012) demonstrated reduced fractional anisotropy of the superior longitudinal fascicle in a group of 10 children, Roberts et al. (2014) reported increased mean diffusivity of the left AF in 14 children with SLI compared to controls. These findings indicate abnormal development of the dorsal language stream in this patient population. We hypothesized that impaired language development in SLI is associated with deficient white matter tracts which transmit information between cortical regions relevant for language. We aimed to investigate a larger pediatric population and to perform a complex assessment of white matter tracts that are related to language processing, including the arcuate fascicle and fiber tracts involved in the ventral stream, which have not been studied in children with SLI previously.

2. Materials and methods

2.1. Participants

A total number of 41 children aged 6–12 years diagnosed with SLI participated in the study. They underwent complex examination including neurological and clinical evaluation, speech-language pathologist assessment and MRI–DTI examination. Parents of participating children answered a comprehensive medical questionnaire covering perinatal history, developmental impairments, neurological and other illnesses. Data from 2 children were excluded due to movement artefacts during MRI scanning. Two children with SLI were excluded due to their age in order to optimize age matching with the control group. Thus, DTI data of 37 children with SLI (8.4 yrs mean age ±1.6 SD, 68% males, 81% right-handed) were analyzed.

For the control group, healthy children aged 6–12 years were recruited by advertisements in nearby schools. Children with a history of language development impairment, hyperactivity, or brain disease and bilingual children were excluded. 43 healthy children underwent the same protocol of magnetic resonance and DTI examination. Data from four controls were excluded due to movement MRI artefacts, two children were excluded because of susceptibility artifacts, and three other children were excluded due to their age in order to optimize the age matching between the groups. This resulted in the analysis of 34 controls (8.9 yrs mean age ±1.6 SD, 53% male, 88% right-handed). Handedness of the participants was reported by parents and confirmed by psychological testing. Parents of children participating in the study gave written informed consent for participation in the study. The study protocol was approved by the Hospital Ethical committee.

2.2. Diffusion tensor imaging

2.2.1. Data acquisition

Diffusion weighted images were collected using a 1.5 T Philips Achieva spin-echo echo planar imaging sequence DTI_NORMAL (echo time TE = 80 ms, repetition time TR = 9480 ms with 15 diffusion directions with a diffusion weighting of $b = 800$ s/mm^2 and one $b0$ volume, 1.58 × 1.58 × 2.5 mm voxels, matrix = 144 × 144, signal averages NSA = 2, 60 slices per volume, SENSE factor of 2. An eight-channel sensitivity encoding SENSE head coil was used. A T2-weighted 3D turbo-spin-echo (TSE) anatomical scan was performed for each subject for anatomical localization of the fiber tracts (repetition time TR = 5000 ms, echo time TE = 45 ms, matrix = 256 × 256, rectangular field of view = 230 mm, slice thickness = 1.5 mm). The imaging sections were positioned to make the section perpendicular to the anterior commissure-posterior commissure line. Total scanning time was approximately 20 min per one subject.

2.2.2. Data processing

Images were processed using FSL tools (FMRIB Software Library v5.0.8) (Smith et al., 2004). Raw diffusion data were converted from DICOM format to NIfTI using dcm2nii software tool and *b*-values and diffusion vectors were extracted during conversion. All diffusion weighted images passed head motion correction, eddy-current correction and brain extraction using FMRIB's Diffusion Toolbox (FDT) and BET FSL-utilities (Smith, 2002).

The B0 diffusion image from each subject was registered with corresponding structural image with higher resolution and then normalized to standard MNI152 space using linear transformation (FLIRT) to provide forward and reverse transformation matrices.

Bedpostx fits the probabilistic diffusion model on the corrected data. Bedpostx was performed by fitting 2 fibers per voxel, which allows for the modeling of crossing fibers. Scalar maps, such as fractional anisotropy (FA), mean diffusivity (MD), mode of the anisotropy (MO) and eigenvalues $\lambda 1$ (axial diffusivity), $\lambda 2$ and $\lambda 3$ maps were generated. Using $(\lambda 2 + \lambda 3)/2$ equation, the radial diffusivity map was calculated.

Tractography was then performed with the use of algorithm implemented in FLS (probtrackx) with 5000 samples, curvature threshold 0.2 (minimal angle approximately 80°). Minimum length threshold was applied differently for each tract: for the arcuate and the uncinate fascicle 50 mm, for IFOF and ILF 100 mm. FA threshold was determined 0.13 as the stop criteria. For tracts detection we used a multiple seed, target and exclude region of interest (ROI) system. ROIs were established and standardized in MNI152 (Montreal Neurological Institute) space.

The ROI system for arcuate fascicle (AF) tracking was identical to the one implemented by Giorgio et al. (2010) and Chen et al. (2015). Given the controversies over the precise location of the origin and termination points of the AF (Dick & Tremblay, 2012), the central white matter portion of the AF was dissected and used for the analysis.

In order to delineate the other tracts we used seed ROI system with respect to Catani's imaging tractography atlas (Catani, Howard, Pajevic, & Jones, 2002; Catani & Thiebaut de Schotten, 2008).

ROIs locations are shown in the Supplementary material.

In the obtained connectivity map diffusion parameters and volumes were calculated for each tract with the use of Matlab scripts (Mathworks Matlab ver.2013a). Tract volumes were calculated from non-zero voxels in the connectivity map multiplied by the voxel size. We set relative thresholds for the connectivity map for the IFOF, ILF and UF as 5% of maximal value, all parameters were estimated again for the thresholded map. All voxels under this threshold were removed from the connectivity map.

In addition, a lateralization index (LI) of the volume was calculated for each tract to assess its inter-hemispheric asymmetry: LI = (LVol − RVol)/(LVol + RVol). This index was normalized and ranged from +1 (maximum left lateralization) to 0 (symmetric) to −1 (maximum right lateralization of the tract). Values of $-0.2 \leqslant LI \leqslant 0.2$ were considered as bilateral (symmetric) findings (Wilke & Lidzba, 2007; Wilke & Schmithorst, 2006).

2.3. Statistical methods

Normality of continuous variables (i.e. age, diffusion parameters and tract volumes) was analyzed by exploring Q–Q graph and Shapiro–Wilk test. Logarithmic transformation was applied for not-normally distributed variables. Levene's test was employed to assess the variance homogeneity of continuous variables. Fisher's